THE HAEMODYNAMIC IMPACT OF ATRIAL FIBRILLATION

STILL SEARCHING FOR THE IDEAL HEART RATE TO TARGET

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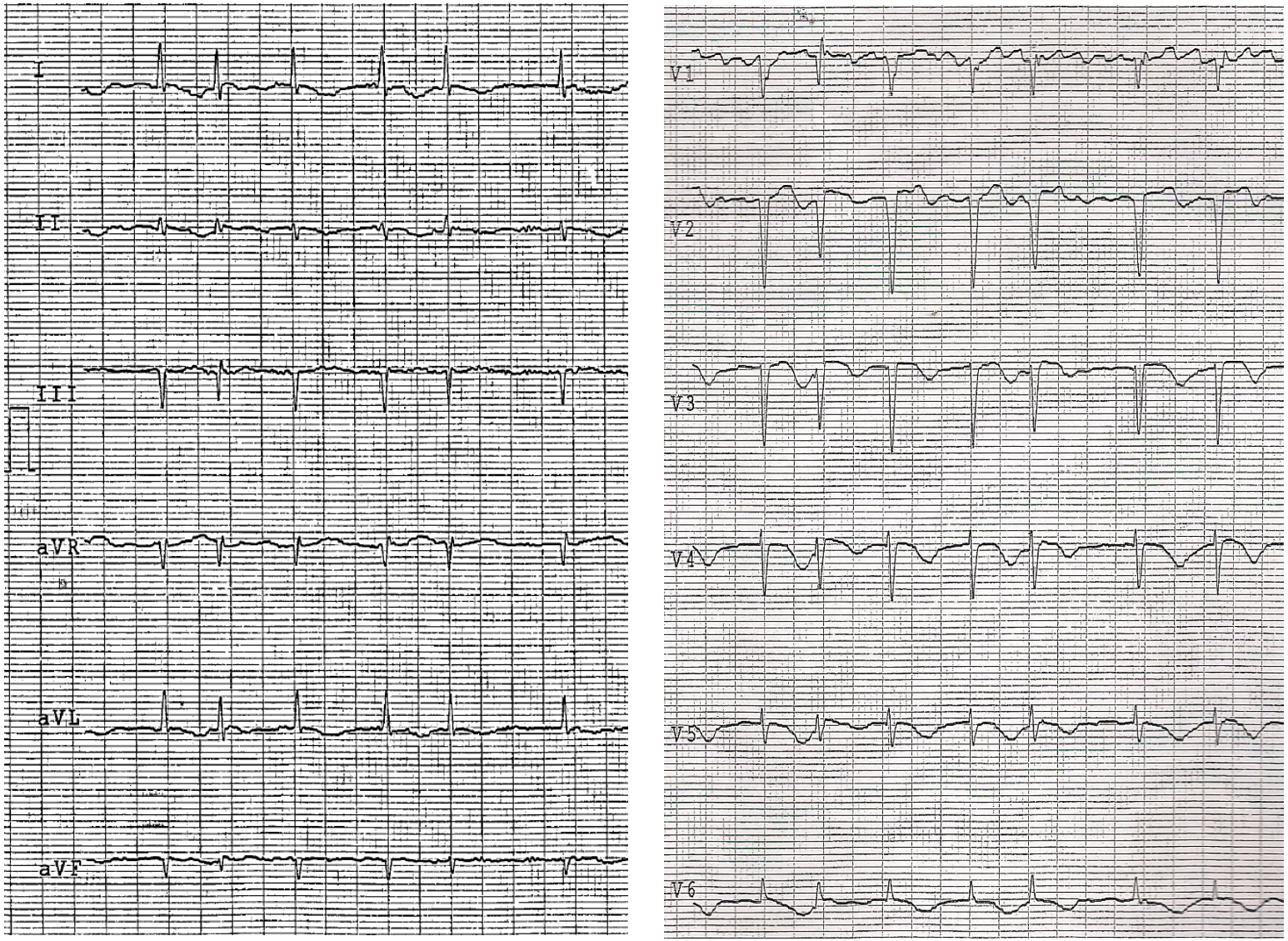
Why that repolarization?



AFib

Neurohormonal activation

Atrial stretch & fibrosis

Altered atrial refractoriness

Heterogeneous conduction

Triggered activity

Volume + pressure overload

HEART FAILURE

Fast ventricular rate

Irregular cycles

Loss of atrial contraction

CARAF (Study on symptoms)

Pts symptomatic	532
Pts asymptomatic	142

Symptoms:	Palpitation	50.7%
	Chest pain	28.6%
	Syncope (or pre)	27.0%

Predictors: young age, high systolic BP, higher HR, female gender, no MI history

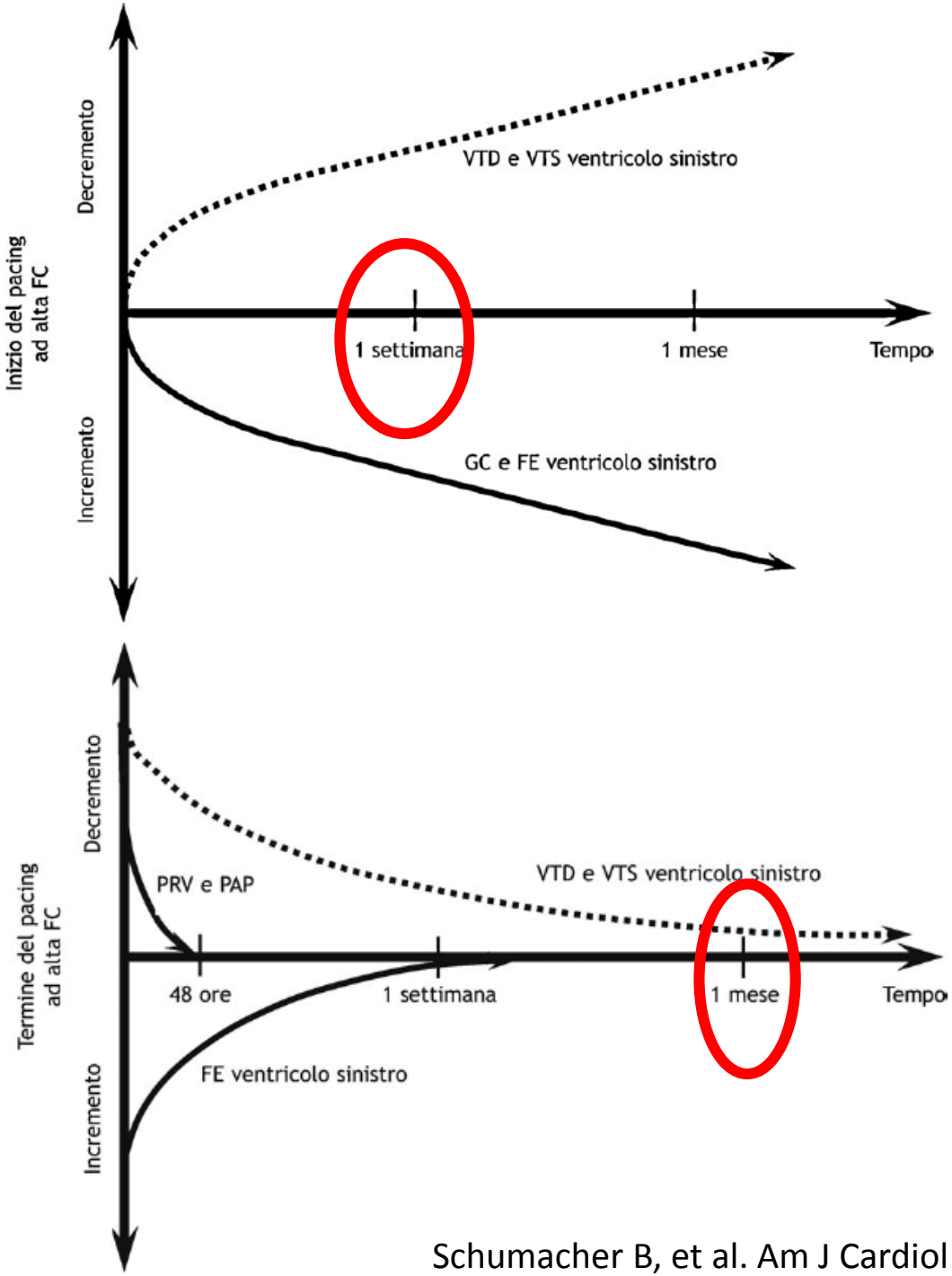
Arrhythmia-Induced Cardiomyopathy (AIC)

A condition in which atrial or ventricular tachyarrhythmias or frequent ventricular ectopy result in LV dysfunction and dilatation, leading to systolic HF.

Usually **REVERSIBLE** (if early recognized and treated)

Arrhythmia induced (pure type):
the arrhythmia is the sole reason for ventricular dysfunction

Arrhythmia mediated (impure type):
the arrhythmia esacerbates ventricular dysfunction and/or worsen HF in a patient with concomitant heart disease



Schumacher B, et al. Am J Cardiol 1998; 82(8A)29-36N

AIC - Proposed mechanisms:

Impaired energy utilization

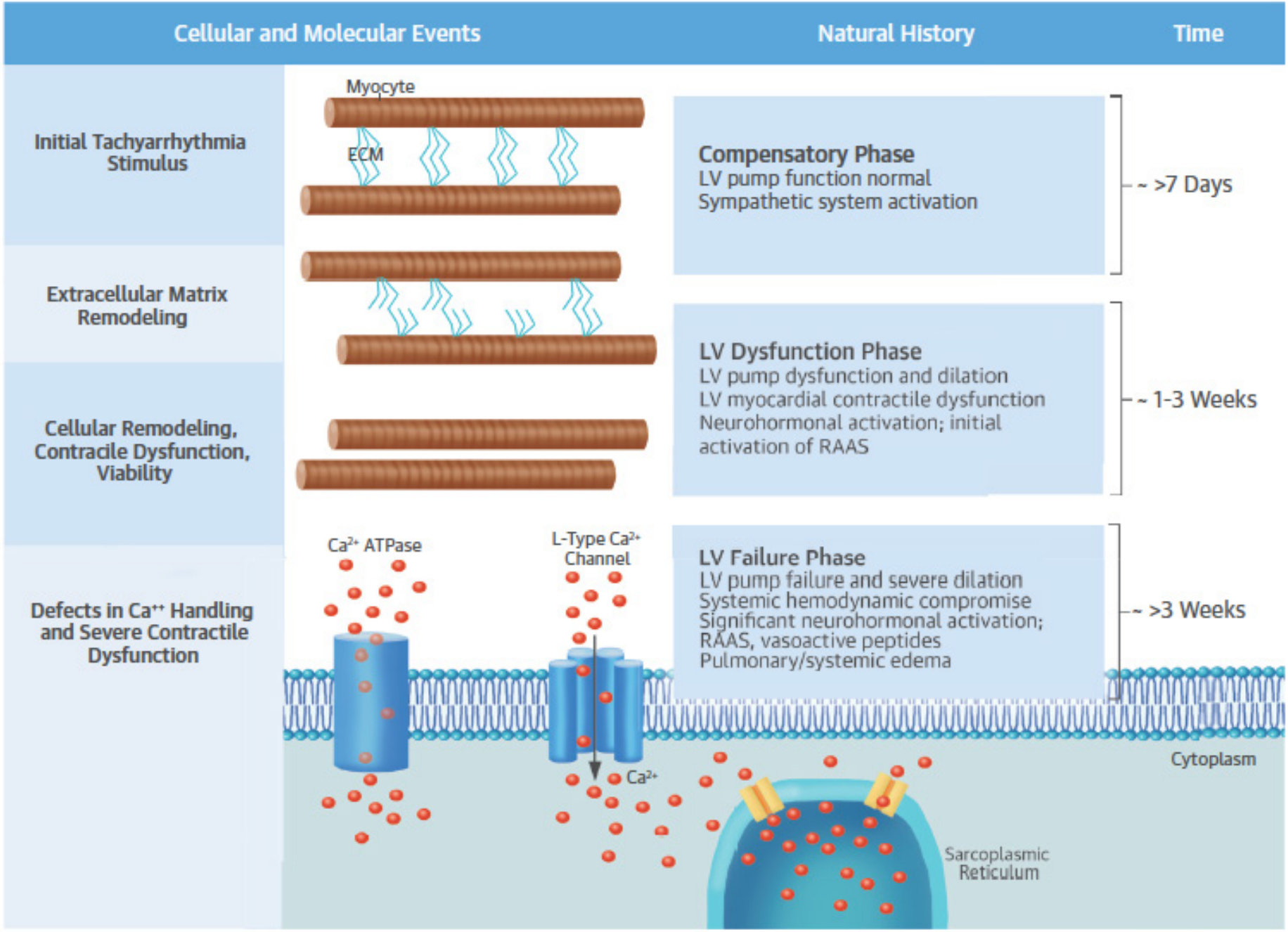
Abnormal calcium handling

Loss of contractile tissue

Functional and structural alteration of mitochondria

Myocardial ischemia (stunning)

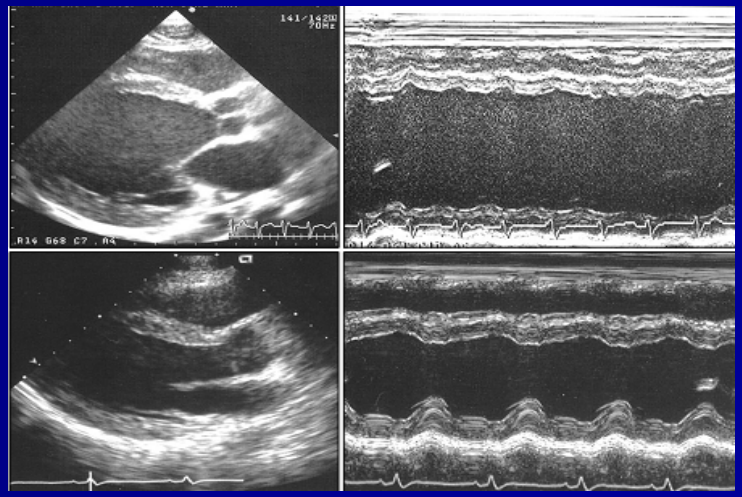
Interstitial fibrosis



Gopinathannair, R. et al. J Am Coll Cardiol. 2015; 66(15):1714–28.

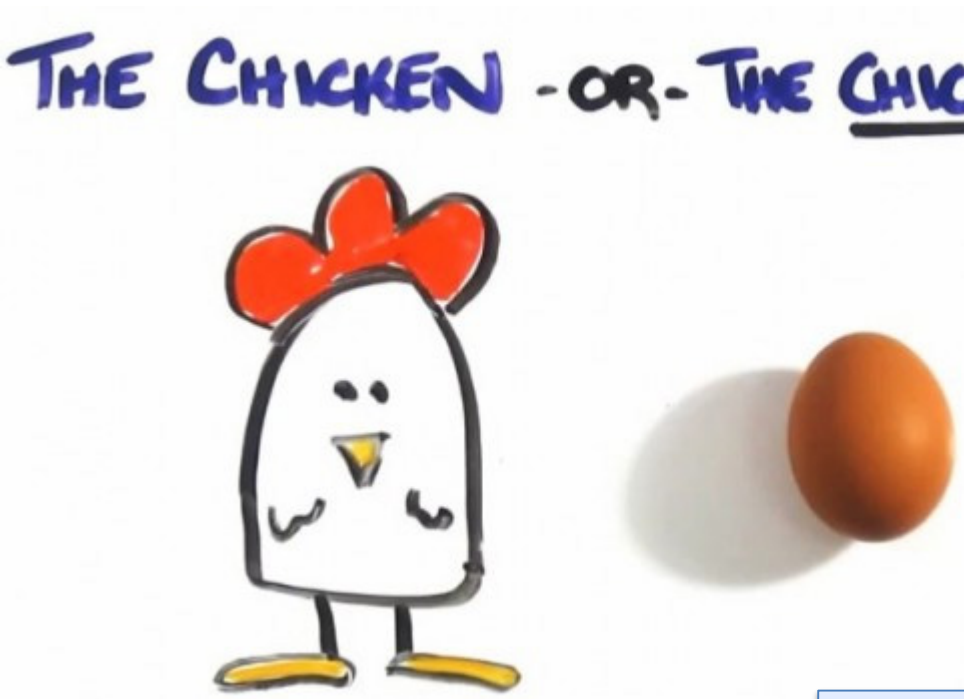
Atrial Fibrillation and Tachycardia Induced Cardiomyopathy

- Tachycardiomyopathy is an impairment in LV function secondary to chronic tachycardia with high and/or irregular ventricular rate leading to HF, which is partially or completely reversible after normalization of heart rate and/or rhythm irregularity
  - Pure type: completely reversible
  - Impure type: partially reversible



- Tachycardiomyopathy is caused by any tachycardia (>110 bpm) persisting more than 10-15% of the day
- Severity is related to rate and duration of ↑ HR
- A correct diagnosis can only be made after a normalization or improvement of the impairment of LV function after control of the tachyarrhythmia.

AIC or otherwise explained cardiomyopathy?



ECHO: smaller LV end-diastolic diameter and mass index in AIC

NT-proBNP at baseline/NT-proBNP during follow-up (NTproBNP ratio) >2.3 at 1 week (suggesting rapid decline in NT-proBNP) is associated with reversible cardiomyopathy.

ECHO-stress:
EF improvement at low doses of dobutamine predicts reversibility.

Cardiac MRI:

- LGE suggesting for underlying scar.
- Abnormal unipolar voltage area (≥32%) of LV endocardium predicts the irreversibility of CMP

Case Report

D.N., M, 76 years old

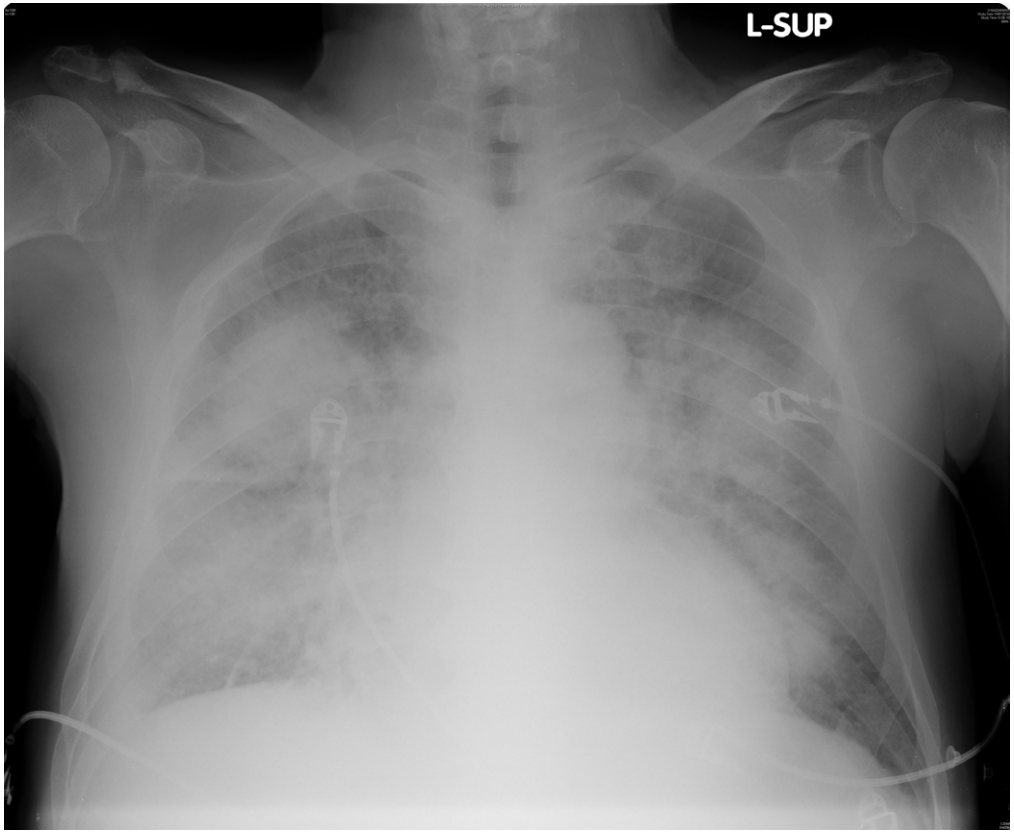
CV risk factor: Hypertension

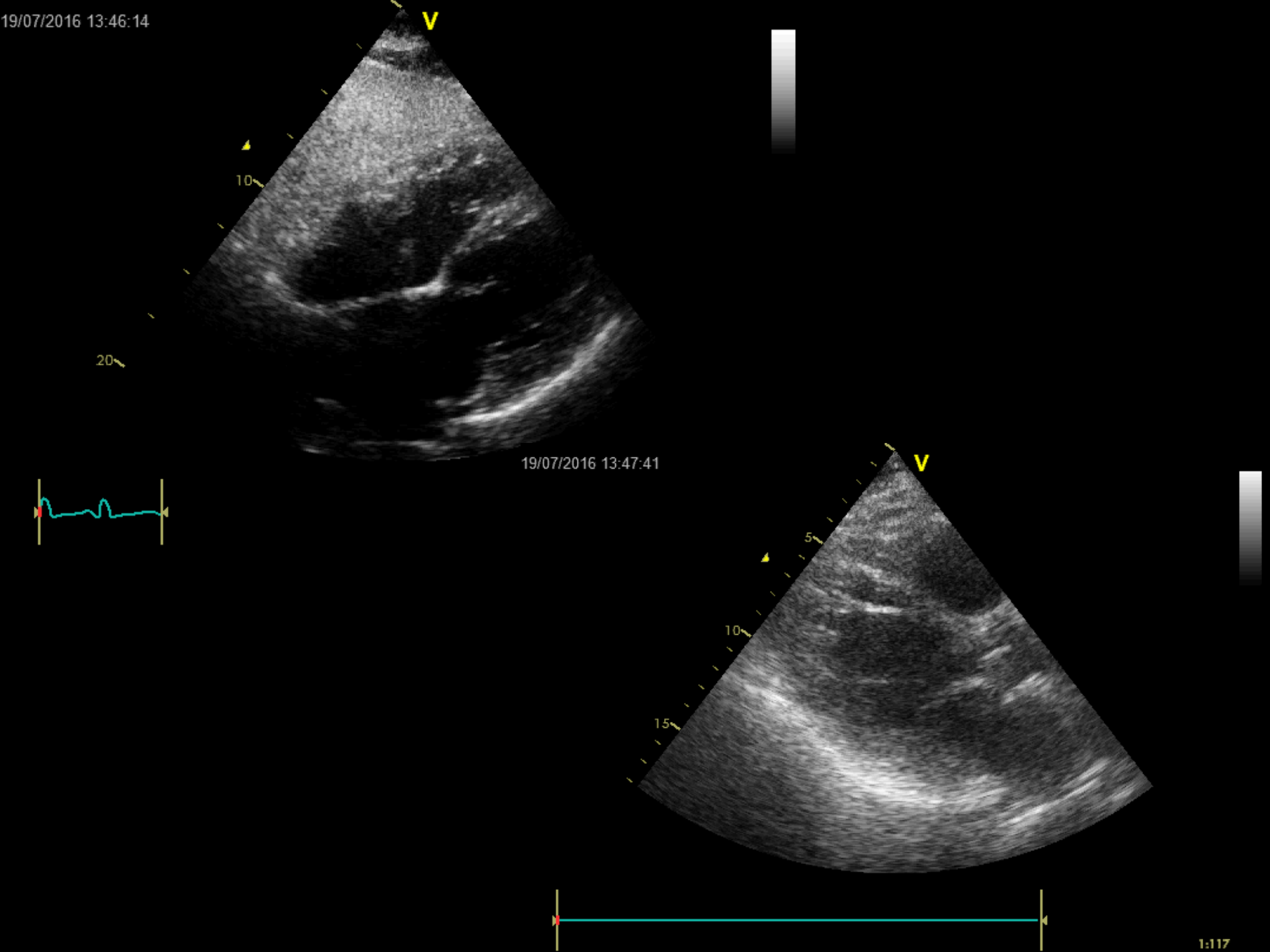
No medical history.

Increasing dyspnea…

Case Report

- Physical examination: pulmonary rales, ankle swelling. 120/80 mmHg
- ECG: AFib, 180/min
- Chest X-Ray:




19/07/2016 13:46:14
V
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Case Report

Rate control (beta-blocker, digitalis)

Antithrombotic therapy (Warfarin)

TEE: Left Atrial Appendage Thrombus

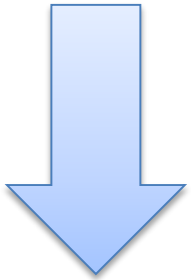
Coronary angiography: no stenosis

Cardiac MRI early stopped (claustrophobia)

Case Report

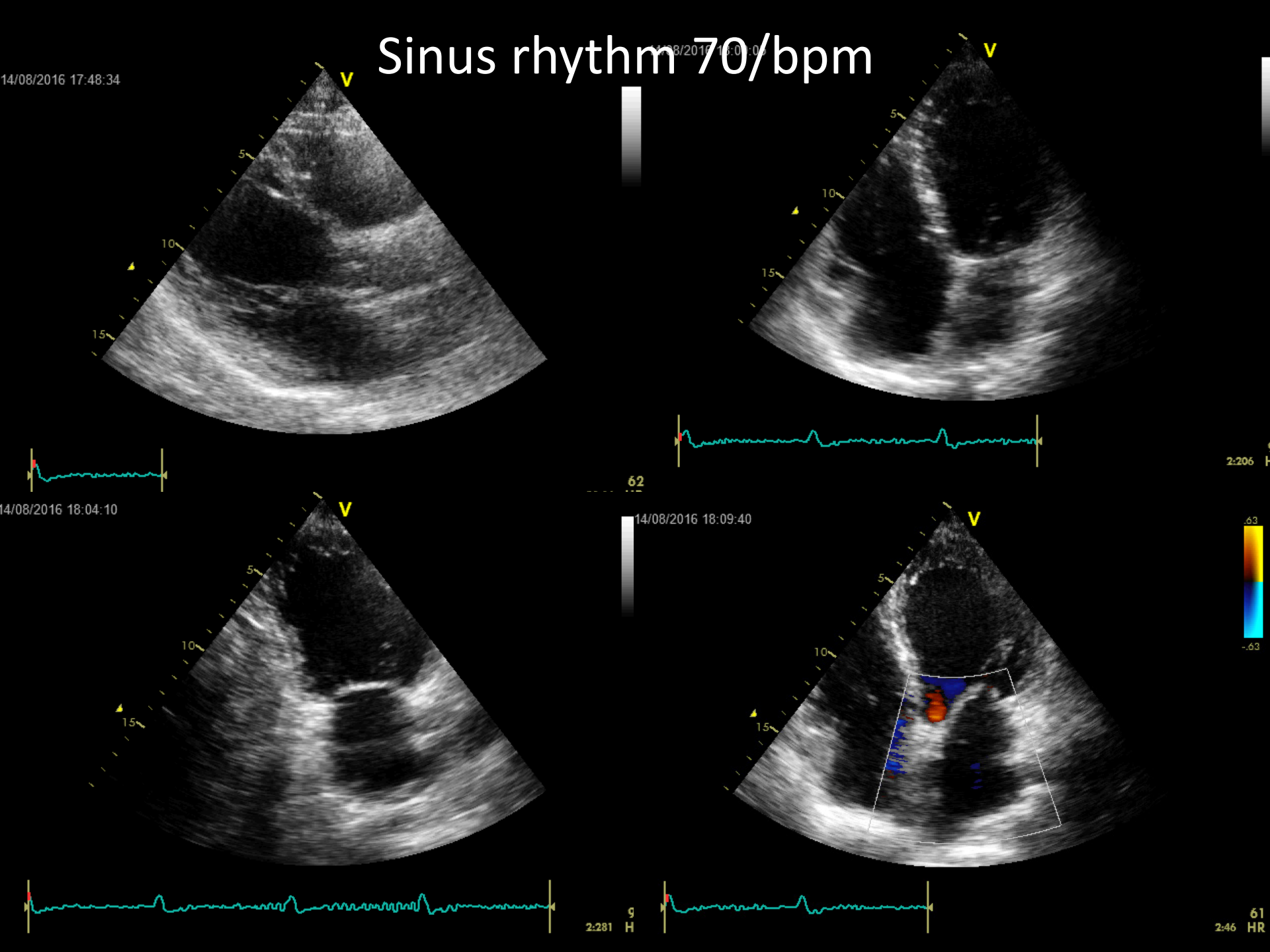
1 month later…

TEE: no more Left Atrial Appendage Thrombus



Electrical cardioversion:SR

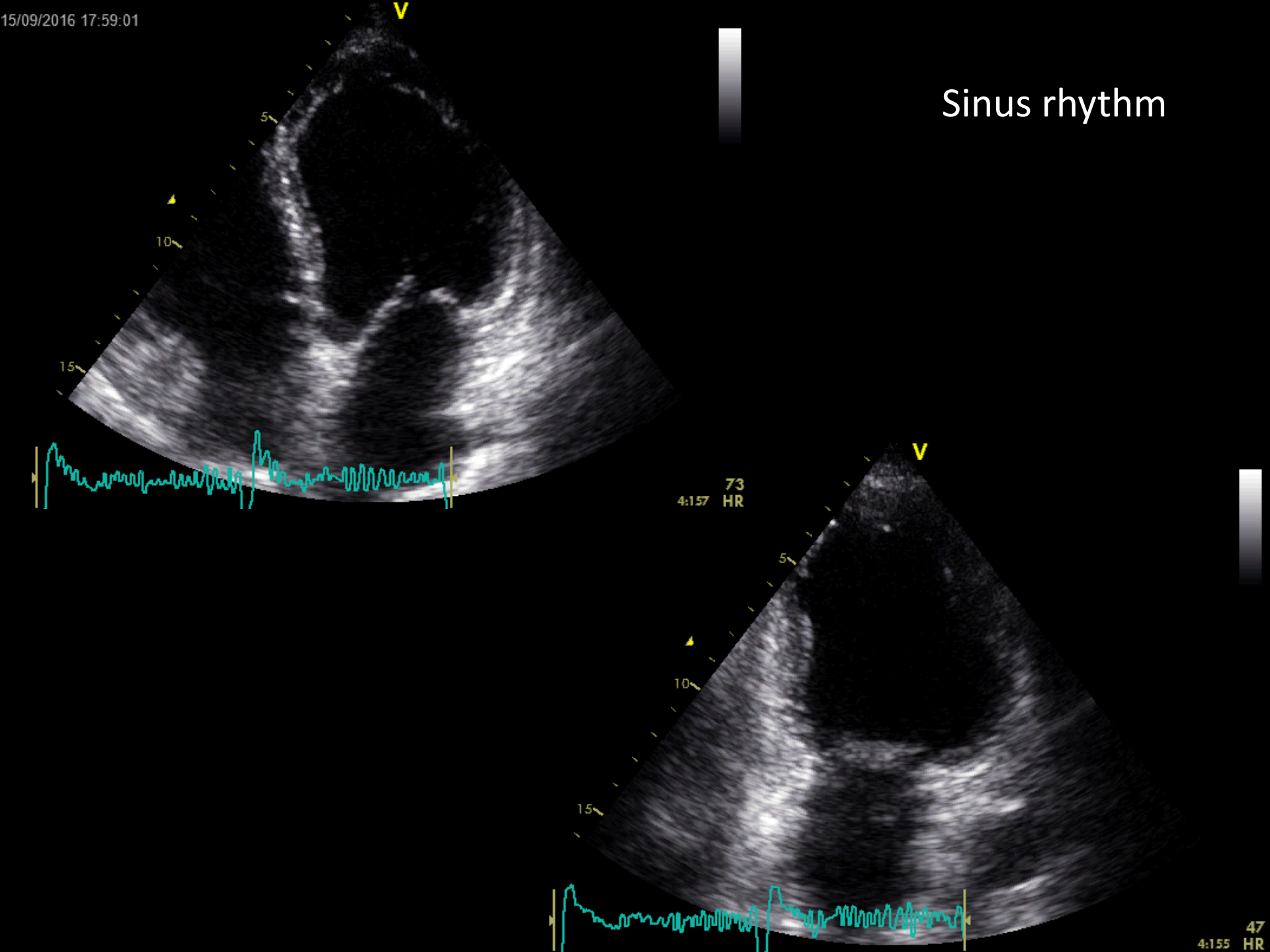
Sinus rhythm 70/bpm



Case Report

Discharged with
Wearable ICD (Life Jacket)

After 2 months of medical therapy, in rhythm control with amiodarone…



Sinus rhythm

RHYTHM vs. RATE CONTROL

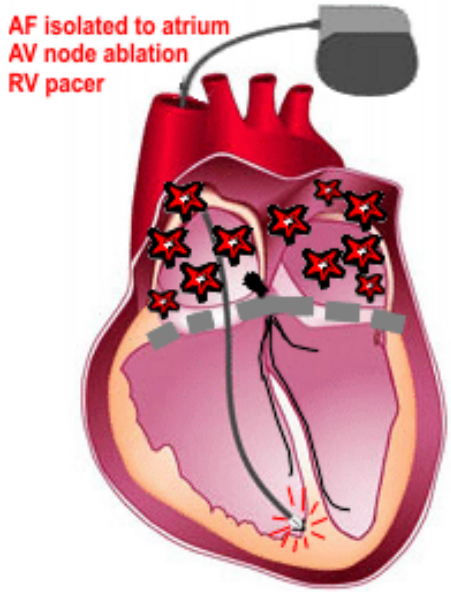


Table 13 General characteristics of rhythm control and rate control trials in patients with AF[86–92]

Trial	Ref	Patients (*n*)	Mean age (years)	Mean follow-up (years)	Inclusion criteria	Primary outcome parameter	Patients reaching primary outcome (*n*)		
							Rate control	Rhythm control	*P*
PIAF (2000)	92	252	61.0	1.0	Persistent AF (7–360 days)	Symptomatic improvement	76/125 (60.8%)	70/127 (55.1%)	0.32
AFFIRM (2002)	86	4060	69.7	3.5	Paroxysmal AF or persistent AF, age ≥65 years, or risk of stroke or death	All-cause mortality	310/2027 (25.9%)	356/2033 (26.7%)	0.08
RACE (2002)	87	522	68.0	2.3	Persistent AF or flutter for <1 years and 1–2 cardioversions over 2 years and oral anticoagulation	Composite: cardiovascular death, CHF, severe bleeding, pacemaker implantation, thrombo-embolic events, severe adverse effects of antiarrhythmic drugs	44/256 (17.2%)	60/266 (22.6%)	0.11
STAF (2003)	88	200	66.0	1.6	Persistent AF (>4 weeks and <2 years), LA size >45 mm, CHF NYHA II–IV, LVEF <45%	Composite: overall mortality, cerebrovascular complications, CPR, embolic events	10/100 (10.0%)	9/100 (9.0%)	0.99
HOT CAFÉ (2004)	89	205	60.8	1.7	First clinically overt persistent AF (≥7 days and <2 years), age 50–75 years	Composite: death, thrombo-embolic events; intracranial/major haemorrhage	1/101 (1.0%)	4/104 (3.9%)	>0.71
AF-CHF (2008)	90	1376	66	3.1	LVEF ≤35%, symptoms of CHF, history of AF (≥6 h or DCC <last 6 months)	Cardiovascular death	175/1376 (25%)	182/1376 (27%)	0.59
J-RHYTHM (2009)	91	823	64.7	1.6	Paroxysmal AF	Composite of total mortality, symptomatic cerebral infarction, systemic embolism, major bleeding, hospitalization for heart failure, or physical/ psychological disability	89/405 (22.0%)	64/418 (15.3%)	0.012

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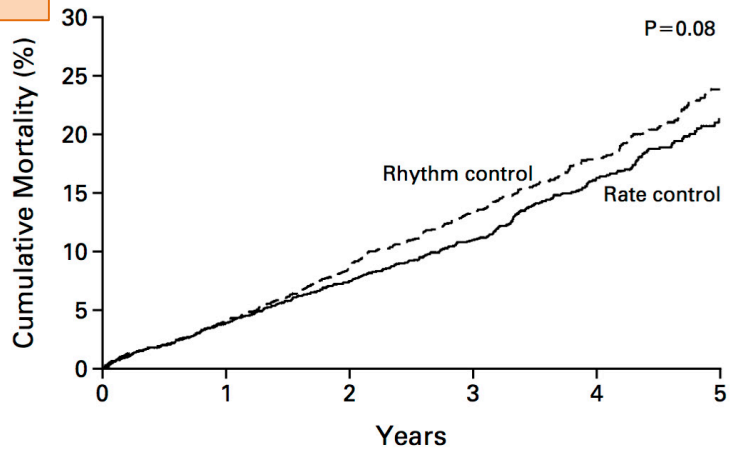
A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION

THE ATRIAL FIBRILLATION FOLLOW-UP INVESTIGATION OF RHYTHM MANAGEMENT (AFFIRM) INVESTIGATORS*

AFFIRM



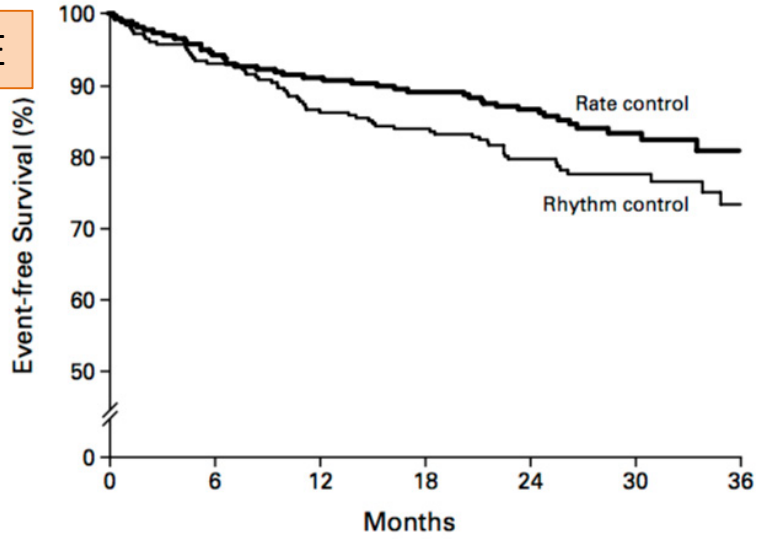
No. of Deaths		number (percent)				
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

Normal LVEF 74% pts.
HR target at rest ≤80 b.p.m.; during daily activity ≤100 b.p.m.

A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH RECURRENT PERSISTENT ATRIAL FIBRILLATION

ISABELLE C. VAN GELDER, M.D., VINCENT E. HAGENS, M.D., HANS A. BOSKER, M.D., J. HERRE KINGMA, M.D., OTTO KAMP, M.D., TSJERK KINGMA, M.SC., SALAH A. SAID, M.D., JULIUS I. DARMANATA, M.D., ALPHONS J.M. TIMMERMANS, M.D., JAN G.P. TIJSSEN, PH.D., AND HARRY J.G.M. CRIJNS, M.D., FOR THE RATE CONTROL VERSUS ELECTRICAL CARDIOVERSION FOR PERSISTENT ATRIAL FIBRILLATION STUDY GROUP*

RACE



No. at Risk							
Rate control	256	239	232	222	212	99	25
Rhythm control	266	243	224	218	207	85	24

Fractional shortening 30±10%

HR target at rest <100 b.p.m.

The NEW ENGLAND JOURNAL of MEDICINE

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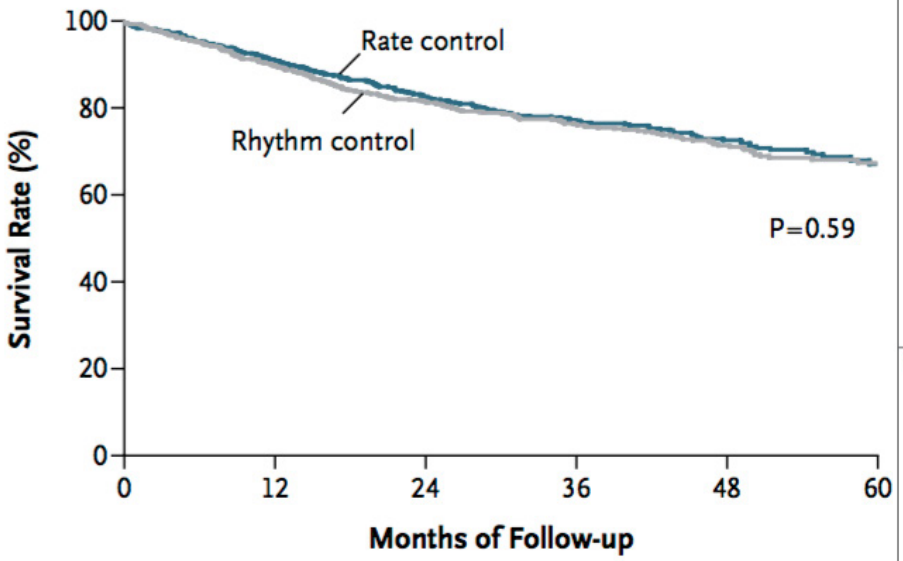
AF-CHF

Rhythm Control versus Rate Control for Atrial Fibrillation and Heart Failure

Denis Roy, M.D., Mario Talajic, M.D., Stanley Nattel, M.D., D. George Wyse, M.D., Ph.D., Paul Dorian, M.D., Kerry L. Lee, Ph.D., Martial G. Bourassa, M.D., J. Malcolm O. Arnold, M.D., Alfred E. Buxton, M.D., A. John Camm, M.D., Stuart J. Connolly, M.D., Marc Dubuc, M.D., Anique Ducharme, M.D., M.Sc., Peter G. Guerra, M.D., Stefan H. Hohnloser, M.D., Jean Lambert, Ph.D., Jean-Yves Le Heuzey, M.D., Gilles O'Hara, M.D., Ole Dyg Pedersen, M.D., Jean-Lucien Rouleau, M.D., Bramah N. Singh, M.D., D.Sc., Lynne Warner Stevenson, M.D., William G. Stevenson, M.D., Bernard Thibault, M.D., and Albert L. Waldo, M.D., for the Atrial Fibrillation and Congestive Heart Failure Investigators*

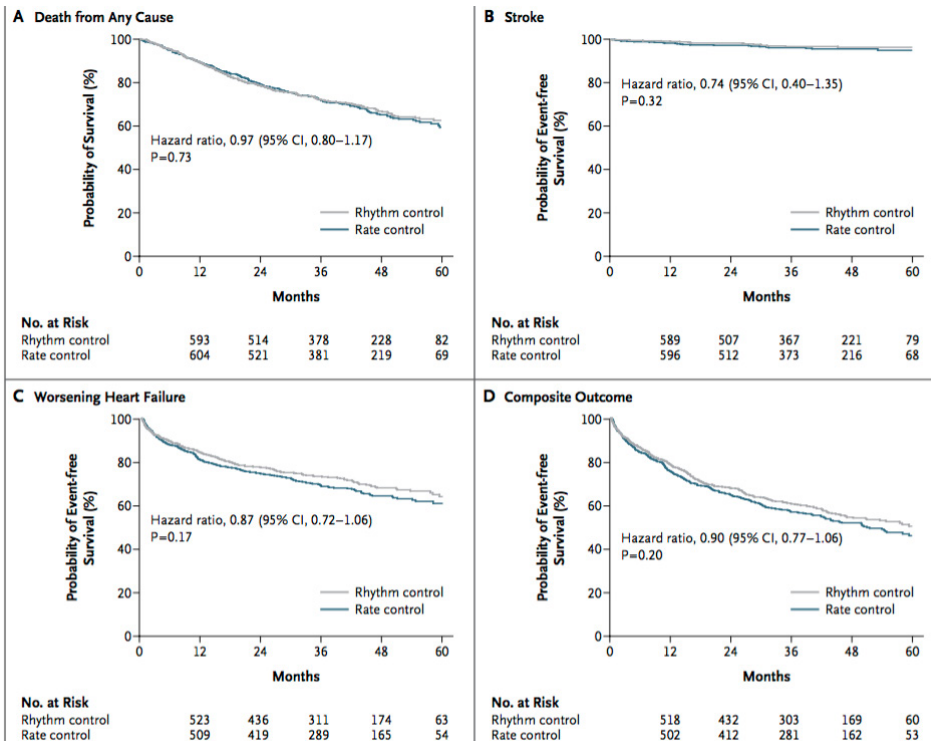
LVEF ≤ 35% (27±6%)

At rest <80 b.p.m.
excercise < 110 b.p.m.



o. at Risk

hythm control	593	514	378	228	82
ate control	604	521	381	219	69



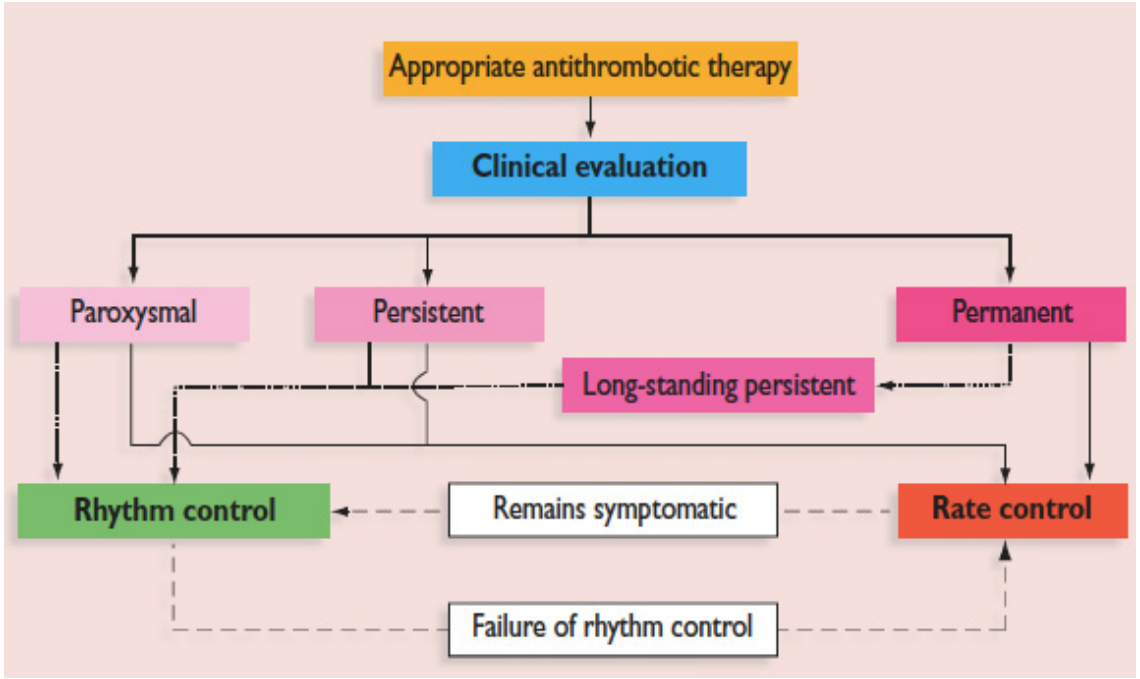
Who need rate control?

1. Background treatment in all patients in atrial fibrillation

2. For patients who do not require sinus rhythm (no or minor symptoms; >80 years)

3. When rhythm control fails

4. When the risks of restoring sinus rhythm outweigh the benefits



What is the ideal HR target

Definitions of ventricular rate control in randomized trials

(Wood MA. Heart Rhythm, 2004)

Study (Reference)	Resting rate (beats/min)	Exercise rate (beats/min)
AFFIRM (3)	<80	<110, with 6-min walk
RACE (4)	<100	Not specified
PIAF (2)	Not specified	Not specified
STAF (1)	Not specified	Not specified
AIRCRAFT (10)	<80	<150 at peak exercise
PAF2	70, lower rate limit	130, upper rate limit

ESC Guidelines AF 2016:

- It is reasonable to initiate treatment with a lenient rate control protocol aimed at a **resting** heart rate **<110 bpm** (class IIaB)
- It is reasonable to adopt a stricter rate control strategy when symptoms persist or tachycardiomyopathy occurs, despite lenient rate control: **resting** heart rate **<80 bpm** and heart rate during **moderate exercise <110 bpm**. (class IIaB)

ESC Guidelines HF 2016:

- a moderately lenient rate control approach aiming at a **resting** heart rate of **60-100** bpm.

AHA/ACC/HRS Guidelines AF 2014:

- A heart rate control (**resting** heart rate **<80 bpm**) strategy is reasonable for symptomatic mangement of AF (class IIaB)
- A lenient rate-control strategy (**resting** heart rate **<110** bpm) may be reasonable as long as patients remain asymptomatic and left ventricular systolic function is preserved (class IIbB)

AHA Guidelines HF 2009:

- target ventricular rate of less than **80-90 bpm at rest** and less than **110-130 bpm** during **moderate excercise**

Canadian AF Guidelines 2014:

- **resting** heart rate **<100** bpm

Post-hoc analysis of AFFIRM study

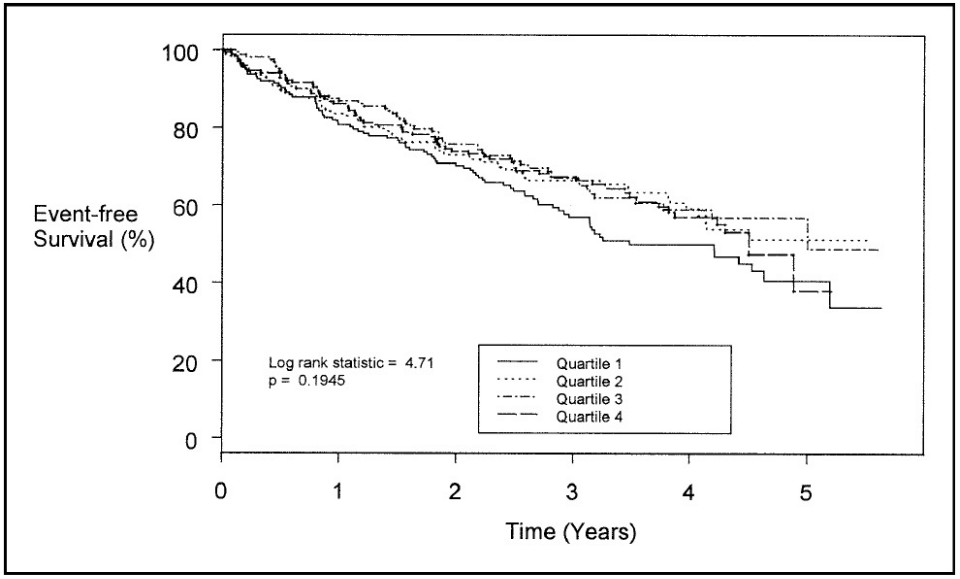


FIGURE 2. Time to death or cardiovascular hospitalization by quartile of achieved HR at rest.

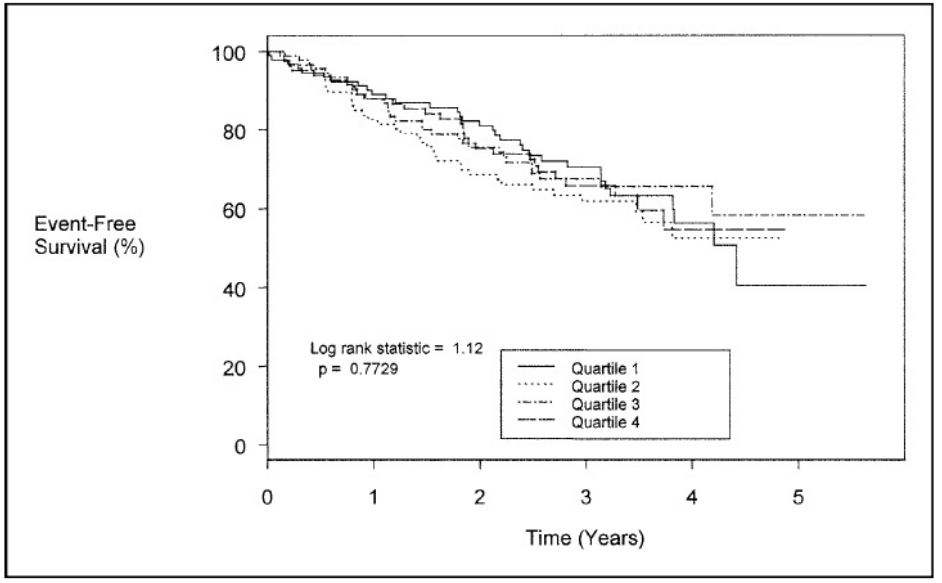


FIGURE 4. Time to death or cardiovascular hospitalization by quartile of achieved exercise HR.

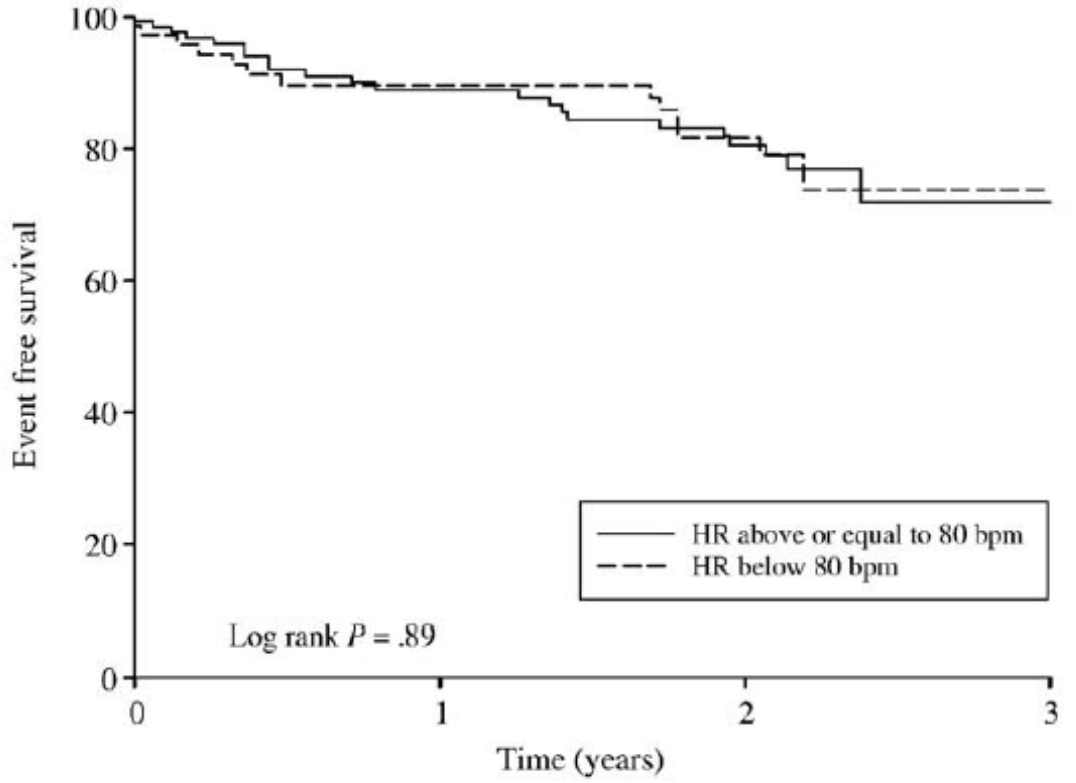
Pts. grouped by quartile of achieved HR
at rest (44-69; 70-78; 79-87; 88-148 bpm)
and achieved exercise HR following a 6MWT
(53-82; 83-92; 93-106; 107-220 bpm)

Cooper, et al. Am J Cardiol 2004;93:1247–1253

Post-hoc analysis of RACE study

Rest HR ≥ 80 b.p.m. (mean 90 b.p.m.)
vs
<80 b.p.m. (mean 72 b.p.m.)

No differences in cardiovascular mortality and morbidity and QoL



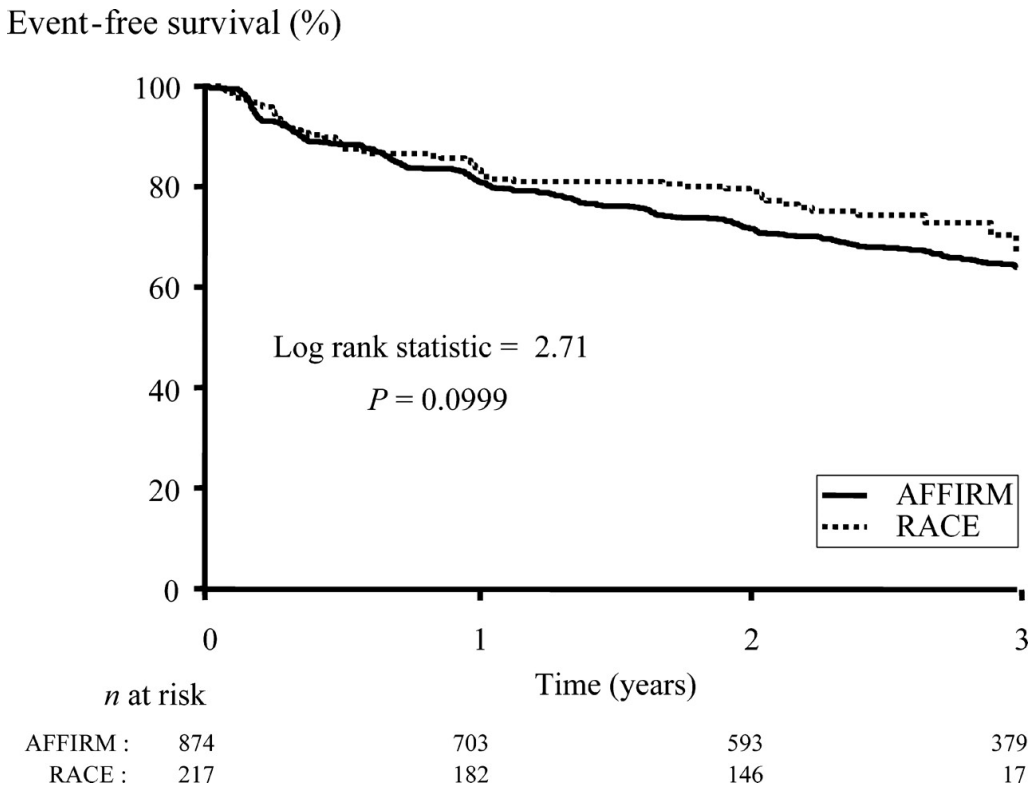
Heart rate <80 bpm (n):			
75	58	39	0
Heart rate ≥80 bpm (n):			
139	86	62	40

Groenveld, et al. American Heart Journal 2009, 158;9: 785-791

Analysis of pooled data from the RACE and the AFFIRM studies

Event free-survival for the primary endpoint (mortality, cardiovascular hospitalization and myocardial infarction) did not differ (64% in AFFIRM vs 66% in RACE)

BUT in the stringent control group the use of pacemaker implantation was higher (11 vs 1%, p=0.0001)



Patients with mean heart rates within the AFFIRM (≤80) or RACE (<100) criteria had better outcome than patients with heart rates ≥100 (HR 0.69 and 0.58 respectively for ≤80 and <100; p 0.004)

Europace (2006) 8, 935–942

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Lenient versus Strict Rate Control in Patients with Atrial Fibrillation

Isabelle C. Van Gelder, M.D., Hessel F. Groenveld, M.D., Harry J.G.M. Crijns, M.D., Ype S. Tuininga, M.D., Jan G.P. Tijssen, Ph.D., A. Marco Alings, M.D., Hans L. Hillege, M.D., Johanna A. Bergsma-Kadijk, M.Sc., Jan H. Cornel, M.D., Otto Kamp, M.D., Raymond Tukkie, M.D., Hans A. Bosker, M.D., Dirk J. Van Veldhuisen, M.D., and Maarten P. Van den Berg, M.D., for the RACE II Investigators*

RACE II

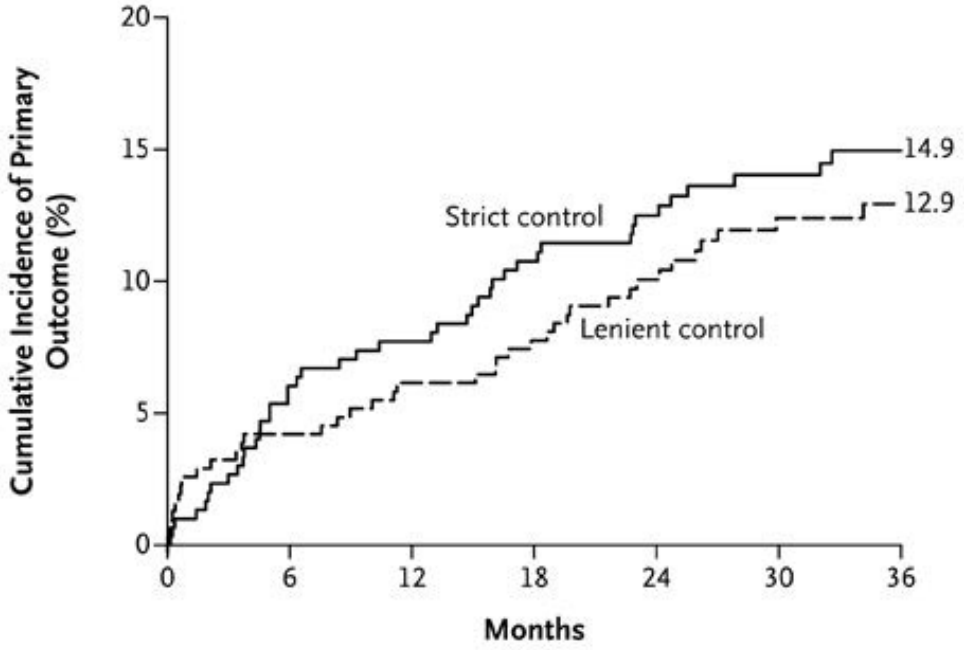
Strict control group: <80 b.p.m at rest, <110 b.p.m. during moderate exercise

vs.

Lenient control group: <110 b.p.m.

No differences in primary composite endpoint, neither NYHA class or hospitalization

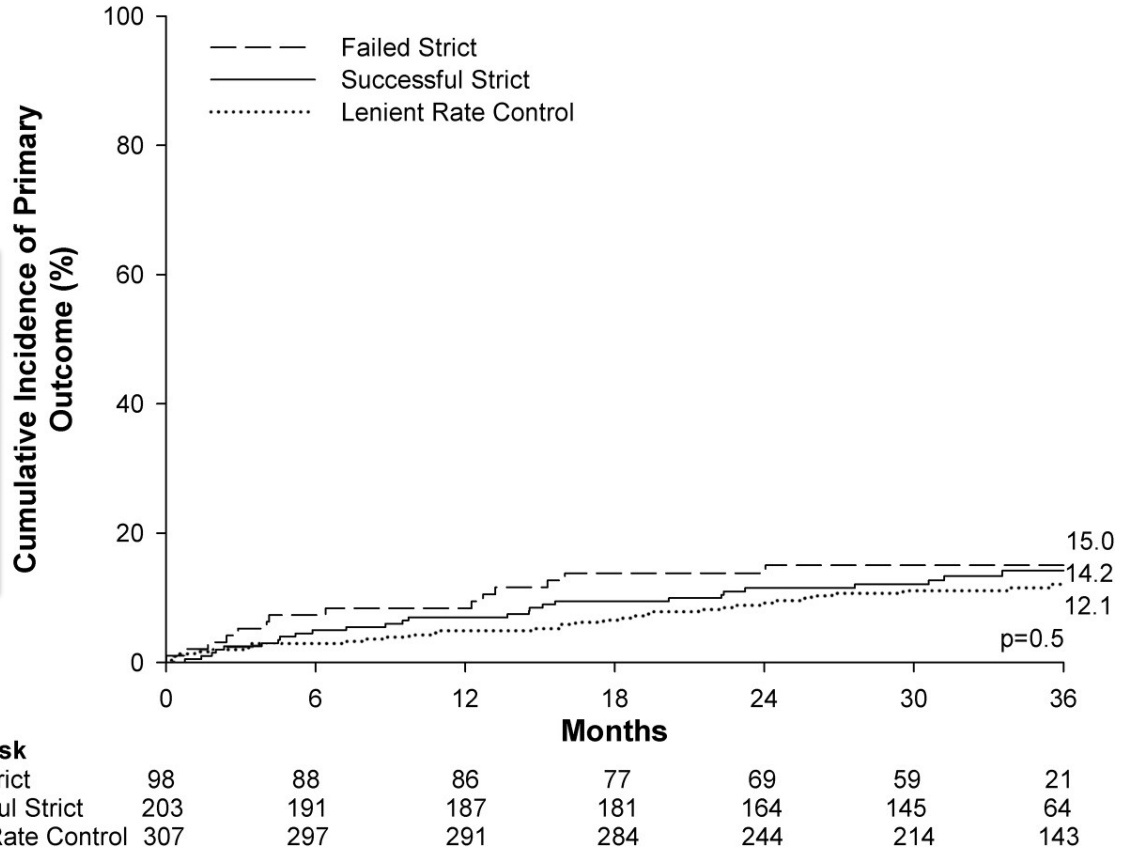
1,4% of the pts. in strict control group needed PMK implantation



No. at Risk							
Strict control	303	282	273	262	246	212	131
Lenient control	311	298	290	285	255	218	138

…. but 33% of the patients in the strict rate control group did NOT achieved the HR target..also the Linient group hardly went over 90 beats/min

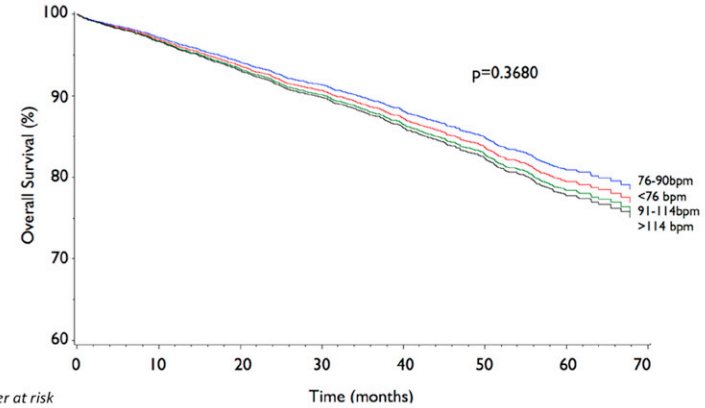
No differences in cardiovascular outcome between successfull strict, failed strict and lenient rate control. QoL was comparable.



Groenveld et al. JACC 2013; 61, 741-8

Pooled data from AFFIRM and AF-CHF

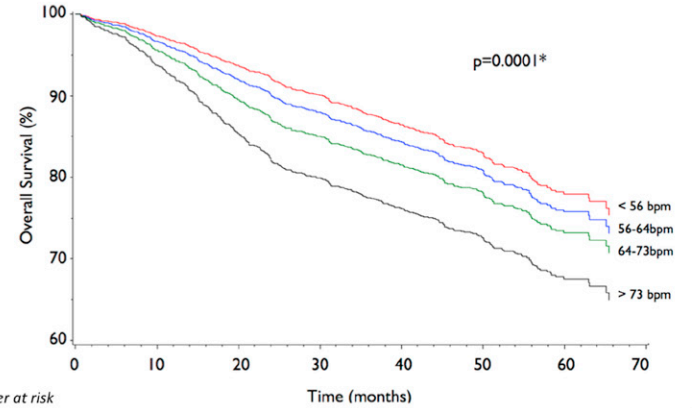
A All-cause mortality: Atrial fibrillation



Number at risk

≤76	1196	1129	1065	890	668	374	138	6
76-90	1086	1039	992	821	574	345	118	6
90-114	1360	1268	1202	1021	754	440	155	8
>114	1206	1150	1100	934	691	442	158	4

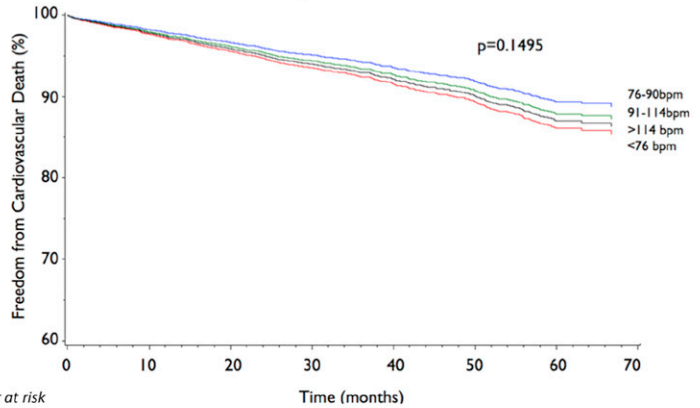
B All-cause mortality: Sinus rhythm



Number at risk

≤56	533	521	499	414	308	193	73	7
56-64	669	644	617	513	374	230	76	5
64-73	533	508	483	401	292	178	72	2
>73	576	535	492	411	318	175	61	0

C Cardiovascular mortality: Atrial fibrillation



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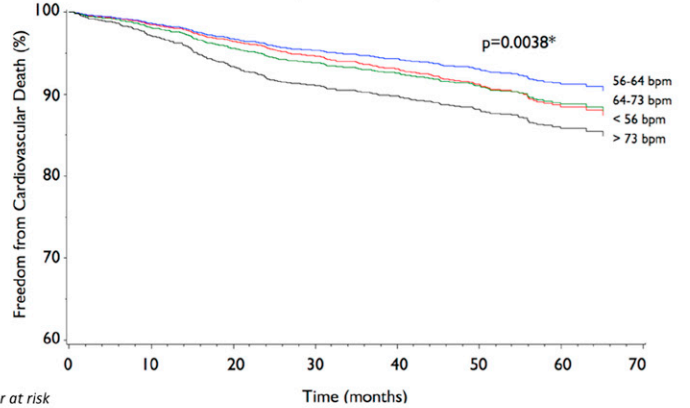
D Cardiovascular mortality: Sinus rhythm



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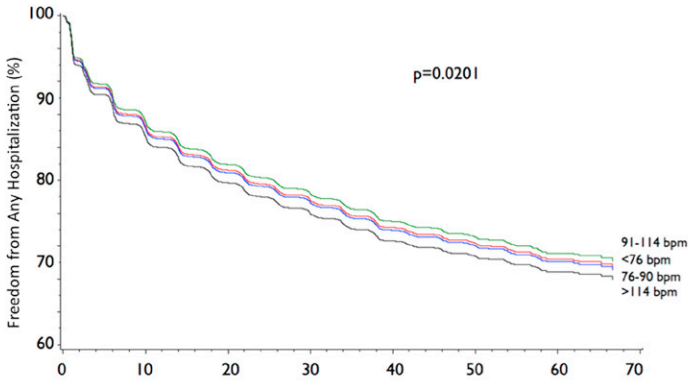
Andrade, et al. Heart Rhythm 2016;13:54-61

Pooled data from AFFIRM and AF-CHF(2)

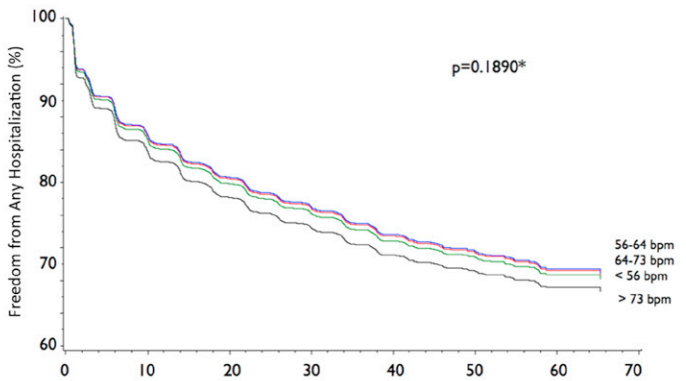
A All-cause hospitalization: Atrial fibrillation



Number at risk

≤76	1196	1039	585	390	232	103	27	1
76-90	1086	684	516	342	195	102	23	2
90-114	1360	861	679	461	282	130	32	0
>114	1206	751	557	372	214	117	26	0

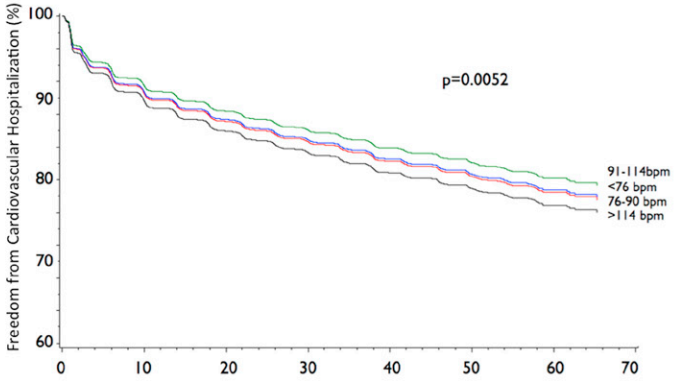
B All-cause hospitalization: Sinus rhythm



Number at risk

≤56	533	314	254	173	115	51	15	1
56-64	669	408	317	208	121	63	18	0
64-73	533	324	242	160	88	44	10	1
>73	576	329	239	155	87	36	5	0

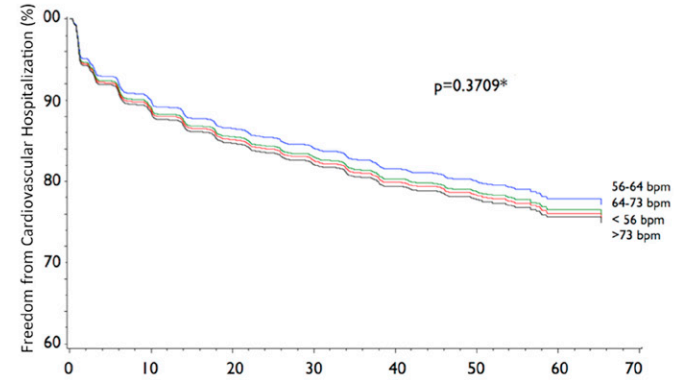
C Cardiovascular hospitalization: Atrial fibrillation



Number at risk

≤76	1196	845	711	511	322	154	41	1
76-90	1086	780	664	476	299	153	41	2
90-114	1360	987	853	623	413	211	54	0
>114	1206	875	729	532	332	194	43	0

D Cardiovascular hospitalization: Sinus rhythm



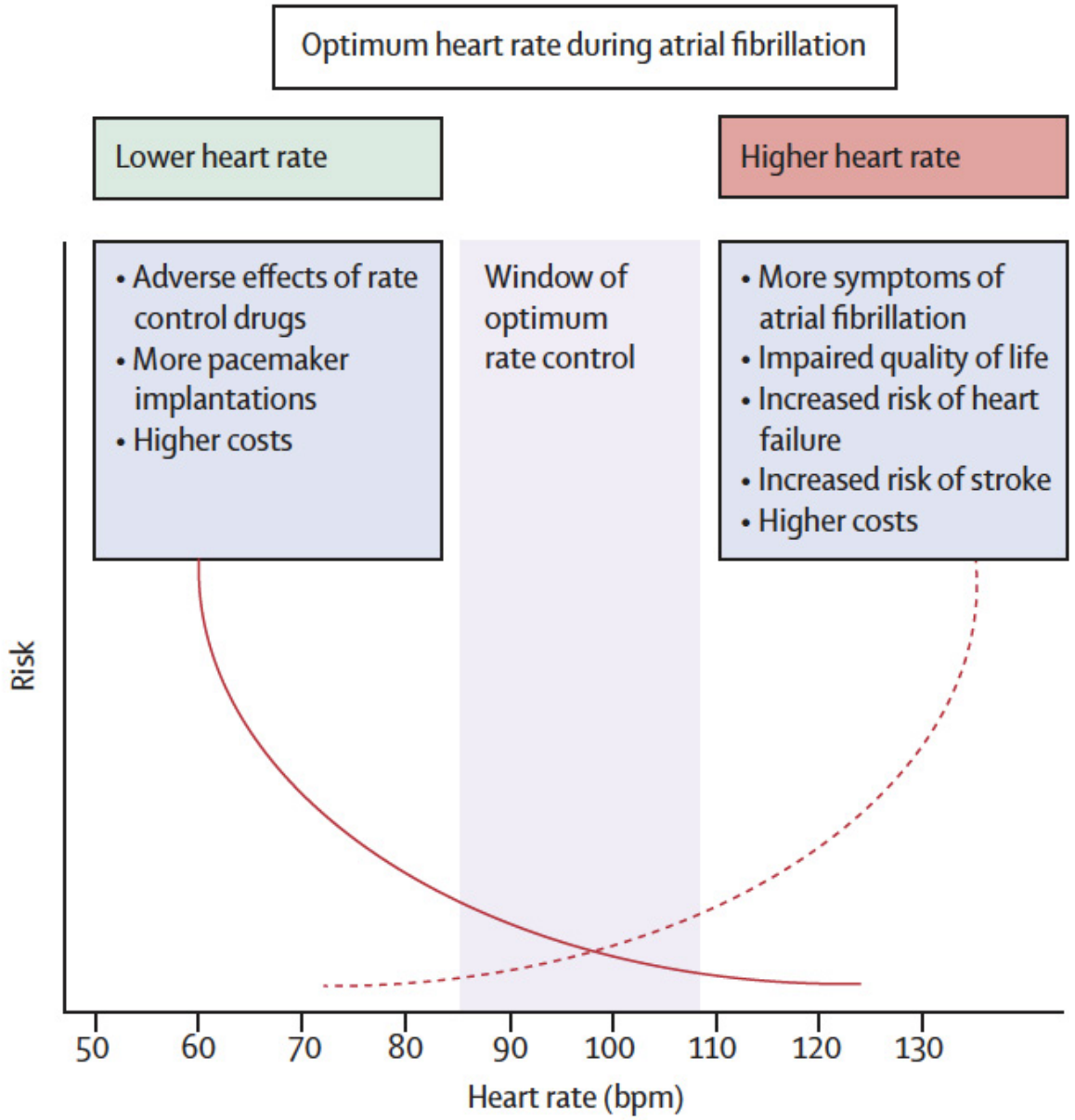
Number at risk

≤56	533	361	311	219	153	73	19	1
56-64	669	464	402	287	189	100	29	0
64-73	533	374	308	225	137	71	22	1
>73	576	385	309	217	132	63	13	0

Andrade, et al. Heart Rhythm 2016;13:54-61

- A high resting heart rate **in sinus rhythm** is significantly and independently associated with an **increased risk of all-cause and cardiovascular mortality**.
- A high heart rate **in AF** is significantly associated with **increased risk of all cause and cardiovascular hospitalization** but not mortality.
- A higher resting heart rate over time is associated with increased all-cause and cardiovascular hospitalization, with largest magnitude of effect observed for heart rates in sinus rhythm.

Association between resting heart rate and adverse cardiovascular outcomes is modulated by the **underlying rhythm**.
The association between resting heart rate in AF and cardiovascular outcomes either was attenuated or altered such **that extremes of resting heart rate** were associated with the greatest risk of hospitalization.



Van Gelder I, et al. Lancet 2016; 388: 818-28

Grazie per l’attenzione